

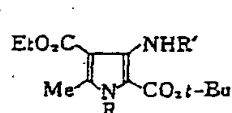
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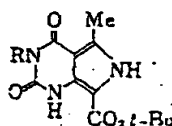
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Facile Synthesis of New Pyrrolo[3,4-d]pyrimidine-2,4-diones

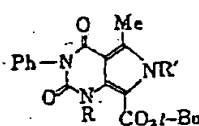
Recently we reported novel syntheses of certain new 3-aminoindoles, pyrido[3,2-b]indoles, pyrrolo[3,2-b]pyridines and pyrrolo[3,2-d]pyrimidines as well as of 3-aminopyrroles, e.g. 1.¹⁾ It is reasonable to predict that 1 can be converted to several pyrrolo[3,4-d]pyrimidine-2,4-diones containing a genuine pyrrole nucleus in the molecules via the corresponding ureas such as 2 or 3, a conventional route, because 1 has a distinct structural feature suitable for the purpose. Since such pyrrolo[3,4-d]pyrimidinediones have never been prepared, they draw our attention by virtue of the structural relationship to 7- and 9-deazapurines. There has been no report of the use of 3-aminopyrroles for pyrrolo[3,4-d]pyrimidine synthesis;²⁾ this is presumably due to the absence of good preparative method for 3-aminopyrroles. The ready availability of 1 facilitated us to fulfil the synthetic approach above suggested.³⁾ We now wish to describe briefly the successful syntheses of new pyrrolo[3,4-d]pyrimidine-2,4-diones (4-10).



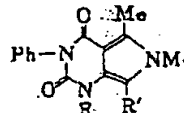
- 1: R=R'=H
 2: R=H, R'=CONHPh
 3: R=H, R'=CONHBu
 11: R=Me, R'=H



- 4: R=Ph
 5: R=Bu



- 6: R=H, R'=Me
 7: R=R'=Me



- 8: R=R'=H
 9: R=Me, R'=H
 10: R=Me, R'=CH2N(Me)2

Ph=phenyl

1 was heated in acetonitrile with phenyl or butyl isocyanate to obtain ureas 2, mp 232° and 3, mp 192-194°, respectively (each in 80% yield). When treated with NaOEt at room temperature, 2 and 3 underwent smooth cyclizations to give the expected products 4, mp 158-159°, ultraviolet (UV) spectrum λ_{max} nm (log ϵ): 240.5 (4.58) and 271.5 (4.28); infrared (IR) spectrum ν_{max} cm⁻¹: 1730, 1696 (shoulder) and 1675 (carbonyls), nuclear magnetic resonance (NMR) spectrum δ (DMSO-*d*₆): 12.20 (NH), 9.16 (NH), 7.1-7.4 (aromatic ring protons), 2.45 (CH₃) and 1.57 (*tert*-C₄H₉), and 5, mp 194-198°, UV λ_{max} nm (log ϵ): 240 (4.51) and 271 (4.25), respectively each in 90% yield. Methylation of 4 with dimethyl sulfato-NaOH in aqueous methanol,⁴⁾ or with dimethyl sulfate-K₂CO₃ in dimethyl sulfoxide (DMSO) yielded 7, mp 230-231°, UV λ_{max} nm (log ϵ): 243 (4.53) and 280 (4.10), IR ν_{max} cm⁻¹: 1709, 1696 and

- 1) a) T. Murata, T. Sugawara and K. Ukawa, *Chem. Pharm. Bull.* (Tokyo), 21, 2571 (1973); b) T. Murata and K. Ukawa, *ibid.*, 22, 240 (1974).
- 2) For the known pyrrolo[3,4-d]pyrimidine syntheses, see P.L. Southwick, R. Madhav and J.A. Fitzgerald, *J. Heterocyclic Chem.*, 6, 507 (1969) and the literatures cited therein; B. Hansen and H. von Döbeneck, *Ber.*, 105, 3830 (1972).
- 3) In the preliminary report we stated that the yield of the 3-aminopyrrole derivative 1 was 70% based on the starting enaminonitrile^{1a)}; however, scrutiny for the better reaction condition has raised the yield. Thus, methyl vinyl ketone (2 ml) was added at 15° to a mixture of the enaminonitrile (27 g) and NaOEt (prepared from 2.5 g of sodium) in ethanol (150 ml); the reaction mixture was stirred for 15 min, concentrated and diluted with water. The resulting crystals of 1 were collected, washed with water and dried. The product weighed 26.5 g (96%).
- 4) G. Nübel and W. Pfeleiderer, *Ber.*, 98, 1060 (1965).